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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HAGOPIAN, CASEY SHEA	
ART UNIT	**PAPER NUMBER**
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Response to Rule 312 Communication	Application No.	Applicant(s)	
	10/766,146	RHEE ET AL.	
	Examiner	Art Unit	
	Casey Hagopian	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

1. ☒ The amendment filed on *01 April 2005* under 37 CFR 1.312 has been considered, and has been:

   a) ☐ entered.

   b) ☐ entered as directed to matters of form not affecting the scope of the invention.

   c) ☐ disapproved because the amendment was filed after the payment of the issue fee.
   Any amendment filed after the date the issue fee is paid must be accompanied by a petition under 37 CFR 1.313(c)(1) and the required fee to withdraw the application from issue.

   d) ☐ disapproved. See explanation below.

   e) ☒ entered in part. See explanation below.

The particular amendment to paragraph 0035 broadens the scope and therefore can not be entered.

CARLOS A. AZPURU
PRIMARY EXAMINER
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Enter In Part
10-6-2005 CA

AMENDMENTS TO THE SPECIFICATION

Please amend the following paragraphs as indicated therein. Deletions are indicated with bold double brackets or a simple strikethrough and additions are underlined.

Ok to Enter in Part 10/05

[0021] Another feature of the invention is that the crosslinked polymer compositions have a high compression strength and high swellability, i.e., a composition that has been dried will swell to three times (or more) its dried size upon rehydration, and is more "elastic." Since these polymers are generally very hydrophilic, they are more easily injected, i.e., the crosslinked composition stays as a "cohesive mass" when injected through a fine ~~gague~~ gauge (27-30 gauge) needle.

[0035] wherein [[m > 2, n > 2, and m + n > 5]] ~~m > 2, n > 2, and m + n > 5;~~ DO NOT ENTER

[0037] [[Y = $-Co_2N(COCH_2)_2$]] Y = $-CO_2N(COCH_2)_2$, $-CO_2H$, -CHO, $-CHOCH_2$, -N=C=O, [[$SO_2CH=CH_2$,]] $-SO_2CH=CH_2$, $-N(COCH)_2$), -S-S-(C_5H_4N), etc., and can be the same or different; and

[0043] [[$(CH_2CH_2O)_n$-]] $-(CH_2CH_2O)_n-$ or $-(CH(CH_3)CH_2O)_n-$ or $-(CH_2CH_2O)_n$ - $(CH(CH_3)CH_2O)_n-$.

[0051] [[$-O_2C-(CH2)_n$-]] $-O_2C-(CH_2)_n-$ polymer - $O_2C-(CH_2)_n$-X (or Y)

[0061] [[polymer - $NH-OCH_2,CH_2CO$ – polymer]] polymer - $NH-OCH_2CH_2CO$ - polymer

[0082] Various forms of multi-amino PEG are commercially available from Nektar ~~Therepeutics~~ Therapeutics, Inc. of San Carlos, CA (through its acquisition of Shearwater Polymers of Huntsville, AL), and from Texaco Chemical Company of Houston, TX under the name "Jeffamine." Multi-amino PEGs useful in the present invention include Texaco's Jeffamine diamines ("D" series) and triamines ("T" series), which contain two and three primary amino groups per molecule, respectively. General structures for the Jeffamine diamines and triamines are shown in Figure 3.

[0083] Polyamines such as ethylenediamine [[$(H_2N-CH_2CH2-NH_2)$]] ($H_2N-CH_2CH_2-NH_2$), tetramethylenediamine [[$(H_2N-(CH_2)_5-NH2)$]] ($H_2N-(CH_2)_4-NH_2$), pentamethylenediamine (cadaverine) ($H_2N-(CH_2)_5-NH_2$), hexamethylenediamine [[(H2N-(CH2)6-NH2)]] ($H_2N-(CH_2)_6-NH_2$), bis(2-hydroxyethyl)amine [[(HN-(CH2CH20H)2)]] ($HN-(CH_2CH_2OH)_2$), bis(2-aminoethyl)amine (HN-

$(CH_2CH_2NH_2)_2$), and tris(2-aminoethyl)amine ($N\text{-}(CH_2CH_2NH_2)_3$) may also be used as the synthetic polymer containing multiple nucleophilic groups.

[0099] As discussed above, preferred activated polyethylene glycol derivatives for use in the invention contain succinimidyl groups as the reactive group. However, different activating groups can be attached at sites along the length of the PEG molecule. For example, PEG can be derivatized to form functionally activated PEG ~~propion aldehyde~~ propionaldehyde (A-PEG), the tetrafunctionally activated form of which is shown in Figure 10, as is the conjugate formed by the reaction of A-PEG with multi-amino PEG. The linkage shown in Figure 10 is referred to as a $-(CH_2)_m$-NH- linkage, where m = 1 - 10.

[0105] Many of the activated forms of polyethylene glycol described above are now available commercially from Nektar ~~Therapeutics~~ Therapeutics and Union Carbide of South Charleston, W.V.

[0115] Polyamines such as ethylenediamine [[($H_2N\text{-}CH_2\ CH_2\text{-}NH_2$)]] ($H_2N\text{-}CH_2CH_2\text{-}NH_2$), tetramethylenediamine ($H_2N\text{-}(CH_2)_4\text{-}NH_2$), pentamethylenediamine (cadaverine) [[($H_2N\text{-}(CH_2),\text{-}NH_2$)]] ($H_2N\text{-}(CH_2)_5\text{-}NH_2$), hexamethylenediamine [[($H_2N\text{-}(CH_2),\text{-}NH_2$)]] ($H_2N\text{-}(CH_2)_6\text{-}NH_2$), bis(2-hydroxyethyl)amine [[($HN\text{-}(CH_2CH_20H)_2$)]] ($HN\text{-}(CH_2CH_2OH)_2$), bis(2)aminoethyl)amine [[($HN\text{-}(CH_2CH_2NH_2)_2$)]] ($HN\text{-}(CH_2CH_2NH_2)_2$), and tris(2-aminoethyl)amine ($N\text{-}(CH_2CH_2NH_2)_3$) can be chemically derivatized to polyacids, which can then be derivatized to contain two or more succinimidyl groups by reacting with the appropriate molar amounts of N-hydroxysuccinimide in the presence of DCC, as described in U.S. Patent No. 5,580,923. Many of these polyamines are commercially available from DuPont Chemical Company.

[0135] Chemically modified collagens[[.]] that are in nonfibrillar form at neutral pH include succinylated collagen and methylated collagen, both of which can be prepared according to the methods described in U.S. Patent No. 4,164,559, issued August 14, 1979, to Miyata et al., which is hereby incorporated by reference in its entirety. Due to its inherent tackiness, methylated collagen is particularly preferred for use in bioadhesive compositions, as disclosed in commonly owned U.S. Patent No. 5,614,587.